AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
P. O. Box 7599
Loveland, Colorado 80537-0599

ATTORNEY DOCKET NO. 10990393-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Jeffrey R. Sampson

Serial No.: 09/358,141 **Examiner: Zara, Jane J.**

Filing Date: July 20, 1999 **Group Art Unit: 1635**

Title: Method of Producing Nucleic Acid Molecules with Reduced Secondary Structure

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria VA 22313-1450

TRANSMITTAL OF REPLY BRIEF

Sir:

Transmitted herewith is the Reply Brief with respect to the Examiner's Answer mailed on April 24, 2006 This Reply Brief is being filed pursuant to 37 CFR 1.193(b) within two months of the date of the Examiner's Answer.

(Note: Extensions of time are not allowed under 37 CFR 1.136(a))

(Note: Failure to file a Reply Brief will result in dismissal of the Appeal as to the claims made subject to an expressly stated new grounds of rejection.)

No fee is required for filing of this Reply Brief.

If any fees are required please charge Deposit Account **50-1078**.

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Respectfully submitted,

Jeffrey R. Sampson

By Cynthia J. Lee

Cynthia J. Lee
Attorney/Agent for Applicant(s)

Reg. No. 46,033

Date: June 26, 2006

Telephone No. (770) 933-9500

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Jeffrey R. Sampson

Serial No.: 09/358,141

Filed: July 20, 1999

Confirmation No.: 1170

Group Art Unit: 1635

Examiner: Zara, Jane J.

Atty. Docket No.: 10990393-1
(50113-1280)

For: **Method of Producing Nucleic Acid Molecules with Reduced Secondary Structure**

REPLY BRIEF TO EXAMINER'S ANSWER
UNDER 37 C.F.R. 41.41

Mail Stop: Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

The Examiner's Answer mailed April 24, 2006 has been carefully considered. In response thereto, please consider the following remarks.

AUTHORIZATION TO DEBIT ACCOUNT

It is not believed that extensions of time or fees for net addition of claims are required, beyond those which may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to deposit account no. 50-1078.

STATUS OF CLAIMS

The following is the status of the claims that are involved in this Appeal:

Claims 1 and 25-35 stand finally rejected. Claims 2-24 are canceled. No claims have been allowed. The final rejections of claims 1 and 25-35 are appealed.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following issue presents the ground of rejection to be reviewed on appeal:

(1) whether claims 1 and 25-35 are anticipated under 35 U.S.C. §102(e) by Vivekananda *et al.* (U.S. Patent 6,569,630, "*Vivekananda*"); and

(2) whether claims 1 and 25-35 are anticipated under 35 U.S.C. §102(e) by Kutyavin *et al.* (U.S. Patent 5,912,340, "*Kutyavin*").

ARGUMENTS

The Examiner has provided in the Examiner's Answer various responses to arguments contained in Applicants' Appeal Brief. In general, Applicants disagree with the position taken by the Examiner in the Examiner's Answer. In this regard, Applicants rely upon the arguments advanced in the Appeal Brief previously filed. However, Applicants offer the following additional comments in reply to the Examiner's Answer. Applicants note for the record that to the extent that every argument presented in Applicants' Appeal Brief that was not addressed in the Examiner's Answer, Applicants incorporate each of those arguments by reference into the present Reply Brief.

A. Related Appeals and Interferences

Applicant's agree with the Examiner that the following appeal is related to the instant appeal: Application No. 09/632,639, Appeal No. 2006-1800 ("the 1800 Appeal"). In the 1800 Appeal, the Examiner's Answer was filed on July 25, 2005 in response to the Appeal Brief filed on May 9, 2005. Further, Applicants filed a Reply to the Examiner's Answer on September 22, 2005 in the 1800 Appeal.

In addition, Applicant identifies the following related appeal: U.S. Application No. 10/423,281, Appeal No. not yet assigned ("the '281 Application"). Since the filing of the Appeal Brief in the instant appeal, a Notice of Appeal was filed in the '281 Application on May 30, 2006. An Appeal Brief has not yet been filed in the '281 Application, which is due to be filed July 30, 2006.

B. Reply to Examiner's Rejection based on *Vivekananda et al.*

Applicant continues to fundamentally disagree with the Examiner's position that claims 1 and 25 –34 are allegedly anticipated by U.S. Patent No. 6,569,630 to *Vivekananda et al.* In addition to the remarks set forth in Applicant's Appeal Brief, Applicant offers the following additional comments, which it hopes will be useful to the Board.

Vivekananda et al. also do not teach methods of synthesizing nucleic acid molecules with reduced levels of cross hybridization. *Vivekananda et al.* disclose a method of detecting anthrax spores and other chemical and biological agents. They achieve this by utilizing nucleic acid molecules that are able to specifically bind particular targets, preferable through non-Watson-Crick interactions. Specifically, *Vivekananda et al.* define their preferred nucleic acid aptamers the following:

> nucleic acid that binds to another molecule ('target' as defined below). This binding interaction does not encompass standard nucleic acid/nucleic acid **hydrogen bond formation** exemplified by Watson-Crick basepair formation (e.g., A binds to U or T and G binds to C), but encompasses all other types of non-covalent (or in some cases covalent) binding.

Column 8, lines 27-33 (emphasis added). The intended binding target of *Vivekananda et al.'s* nucleic acids are "any compound or aggregate of interest. Non-limiting examples include a protein, peptide, carbohydrate, polysaccharide, glycoprotein, lipid, hormone, receptor, antigen, allergen, antibody, substrate, metabolite, cofactor, inhibitor, drug, pharmaceutical, nutrient, toxin, cholera toxin, Shiga-toxin, poison, explosive pesticide, chemical warfare agent, biohazardous agent, prion, radioisotope, vitamin, heterocyclic aromatic compound, carcinogen, mutagen, narcotic, amphetamine, barbiturate, hallucinogen, waste product, contaminant, or other molecule." Column 8, lines 46-56. Thus, *Vivekananda et al.* do not teach a method of synthesizing nucleic acids with reduced levels of cross hybridization, but instead teach a method

of synthesizing nucleic acids that bind to their intended non-nucleic acid targets with greater affinity via non-Watson-Crick-type interactions.

By contrast, Claim 1, for example, is directed to a method of synthesizing an unstructured nucleic acid molecules that includes "a first complementary nucleotide that hybridizes with a first residue within the first sequence element on the template strand and a second complementary nucleotide that hybridizes with a second residue within the second sequence element on the template strand, wherein the first and second residues are complementary to one another but the first and second nucleotides have a reduced ability to form a stable **hydrogen bonded** base pair." (emphasis added).

Thus, the presently pending claims recite the synthesis of nucleic acid molecules that do bind to certain nucleic acid molecules via traditional Watson-Crick-like hydrogen bonding interactions (*i.e.*, "a first complementary nucleotide that hybridizes with a first residue within the first sequence element on the template strand and a second complementary nucleotide that hybridizes with a second residue within the second sequence element on the template strand" of claim 1). *Vivekananda et al.* simply do not teach or suggest such a method. Instead, by stating that their invention "does not encompass standard nucleic acid/nucleic acid hydrogen bond formation" (col. 8, lines 28-20), *Vivekananda et al.* actually teach away from the currently pending claims, and thus cannot anticipate the present claims.

Because *Vivekananda et al.* at least fail to teach at least these element of the claims, independent claim 1 is not anticipated under 35 U.S.C. § 102(e) by *Vivekananda et al.* Applicant respectfully requests that the Board overturn the rejection.

In addition and notwithstanding the foregoing, the only application that the *Vivekananda et al.* reference claims priority to that pre-dates the filing date of Applicant's instant application

is *Vivekananda et al.*'s U.S. provisional application serial no. 60/142,301 ("the '301 Provisional"). It has come to Applicant's attention that, after a careful review of the '301 Provisional, none of the features relied on by the Examiner in the *Vivekananda et al.* reference are present in the '301 Provisional. Therefore, for at least the reason that Applicant's invention was not described in an application for patent that was filed before Applicant's application for patent, the rejection based on *Vivekananda et al.* should be overturned.

C. Reply to Examiner's Rejection based on *Kutyavin et al.*

Applicant continues to fundamentally disagree with the Examiner's position that claims 1 and 25 –35 are allegedly anticipated by U.S. Patent No. 5,912,340 to *Kutyavin et al.* In addition to the remarks set forth in Applicant's Appeal Brief, Applicant offers the following additional comments, which it hopes will be useful to the Board.

Claims 1 recites a "a collection of nucleotides sufficient to synthesize a nucleic acid strand complementary to at least a portion of the template nucleic acid strand." Thus, claim 1 recites an unstructured single-stranded nucleic acid molecule. This feature is not taught or suggested by *Kutyavin*. The Office Action alleges that both members of a non-hydrogen bond forming nucleotide pair, present in each nucleic acid molecule produced, is disclosed by *Kutyavin*. *See, e.g., Examiner's Answer* at 10. However, every citation and every example that is cited by the Office in *Kutyavin*, in Applicant's view, discusses the matched pair of the Selective Binding Complementary Oligonucleotides (SBC ODNs) being present in a manner that is complementary "to a target duplex sequence..." and that "[t]he ODNs form substantially stable hybrids with the target sequence in each strand of the duplex nucleic acid." *Kutyavin* at col. 1, lines 39-67 (emphasis added). Because the ODNs form hybrids with each strand of the target duplex

sequence, this necessitates that the ODNs be present as a pair of nucleic acid molecules. Even one of the examples cited by the Examiner (Hybrid IV in Table 1 of *Kutyavin*) comprises "two 28-mer sequences", wherein "each member of this pair forms a stable hybrid with its natural complement." *Kutyavin* at col. 23, lines 30-54 (emphasis added).

Referring again to Exhibit A of the Appeal Brief, Scheme B illustrates the following passage of *Kutyavin*:

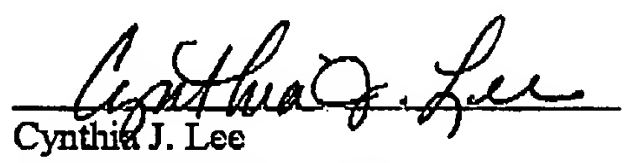
> In case of long double stranded DNA, sequentially hybridizing the paired SBC ODNs to each member of the DNA target and then combining these hybrids results in stable double D loop formation which is stabilized by the bonding between each member of the SBC ODN pair and the corresponding complementary sequence in the target DNA.

Kutyavin at col. 24, line 66 – col. 25, line 5 (emphasis added). *Kutyavin* discloses double strand invasion with two strands of the SBC ODNs. Thus, the feature of claim 1 of a single-stranded unstructured nucleic acid is not taught or suggested by *Kutyavin*.

CONCLUSION

In summary, it is Applicant's position that Applicant's claims are patentable over the applied prior art references and that the rejection of these claims should be withdrawn. Appellant therefore respectfully requests that the Board of Appeals overturn the Examiner's rejection and allow Applicant's pending claims.

Respectfully submitted,



Cynthia J. Lee
Registration No. 46,033

THOMAS, KAYDEN, HORSTEMEYER & RISLEY, LLP
100 Galleria Parkway, N.W.
Suite 1750
Atlanta, Georgia 30339
(770) 933-9500

00390590